

AD _____

Award Number: DAMD17-94-J-4343

TITLE: Breast Cancer Tissue Repository

PRINCIPAL INVESTIGATOR: J.Dirk Iglehart, M.D.

CONTRACTING ORGANIZATION: Duke University Medical Center
Durham, North Carolina 27710

REPORT DATE: September 1999

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20010216 132

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE September 1999		3. REPORT TYPE AND DATES COVERED Final (1 Sep 94 - 31 Aug 99)	
4. TITLE AND SUBTITLE Breast Cancer Tissue Repository"				5. FUNDING NUMBERS DAMD17-94-J-4343	
6. AUTHOR(S) J. Dirk Iglehart, M.D.					
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Duke University Medical Center Durham, North Carolina 27710 E-MAIL:				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES					
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited					12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) <p>The Breast Tissue Repository at Duke University completed its fourth and final year of funding and was granted a no-cost extension to continue its mission for one additional year (from 9/98-9/99). This report highlights work performed under this no-cost extension year and constitutes the final report on the grant.</p> <p>This resource was designed to: 1.) provide freshly frozen tumor tissue from primary and metastatic sites (lymph nodes) for exploratory research, 2.) collect serum and plasma from patients and controls, and 3.) collect white blood cells from patients and controls. During the past year, we collected tumor tissue from 65 patients, 119 patients donated pre-operative blood samples, and 5 specimens were collected in a sterile fashion for special studies. We provided investigators at Duke and collaborating centers with more than 100 samples of frozen breast tumors. In each case, the quality of the tissue was determined by frozen section analysis and macrodissection done to enhance the fraction of the tissue specimen which contained malignancy. Blood samples were distributed to investigators at Duke and sent to collaborators in other institutions. We have applied for administrative continuation (without funding) to continue the process of serial blood collection from patients already consented and who have already provided a first blood sample. As a partial indication of the success of this bank, we competed for and received a Planning Grant in Breast Cancer from the NCI in 1994. A SPORE in Breast Cancer was awarded in 1995 and a Cancer Genetics Network grant started in 1998.</p>					
14. SUBJECT TERMS Breast Cancer				15. NUMBER OF PAGES 8	
				16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited		

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

Table of Contents

Introduction.....	page 3
Body.....	page 4
Key Research Accomplishments	page 6
Reportable Outcomes.....	page 6
Conclusion	page 6
References.....	page 6
Appendices.....	page 6
Final Report	page 6

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

X Where copyrighted material is quoted, permission has been obtained to use such material.

X Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

X Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

X For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

N/A In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

PI - Signature

Date

12/14/85

Introduction

The Breast Cancer Tissue Repository at Duke University Medical Center is a US Army-funded infrastructure project. Our project began in 1994 and we have just completed our fourth and final year. We have had continuous Institutional Review Board approval for this project. Informed consent was obtained from each patient and is kept in files within the Multidisciplinary Breast Program office and within the offices of the Principal Investigator. We have more than 600 separate consents for the donation of blood. The donation of tissue is covered by the global informed consent document given to all patients going to surgery at Duke. The IRB approval for tissue acquisition is held by the Chairman of Surgery at Duke Hospital. We have collected specimens from 424 separate patients during the past four years.

The philosophy of our resource was unique. We encouraged the rapid use of our tissues by investigators seeking validation of hypotheses or performing exploratory, hypothesis generating studies. Our Repository was not designed for long-term follow-up studies and did not include an extensive clinical history database. However, we did construct a data management system that was used to inventory the bank and to provide detailed information about pathology. Anonymous linkage to the Cancer Center tumor registry was available for those investigators who requested this information. We were committed to providing large amounts of tissue to investigators with only a brief justification for its use. As the list of our users shows, this was a very mature and productive group of people.

We also provided special services to investigators who needed it. This was particularly true for scientists on the Duke Campus. Blood collection from special groups of patients and tissue collection in special ways was done for several groups of scientists. For instance, we provided "on-call" services to the Duke SPORE for a project concerned with genetic counseling about BRCA1 and BRCA2 testing. Patients were given the option of testing at Duke, for free, and part of the counseling research. In this circumstance, blood needed to be drawn and delivered to the testing laboratory immediately and confidentially. The US Army Repository phlebotomist was available to obtain the blood and deliver it immediately to the testing laboratory.

We have now reached the final year of funding. However, because of the DOD grant, we have been successful in securing continuing funding for this activity. In 1994, we were awarded an NIH Planning Grant in Breast Cancer. In 1995, we received a SPORE in Breast Cancer from the NCI. This year, we won a Cancer Genetics Network grant. These, and other sources, will allow us to continue the invaluable work of collecting, storing and distributing human tissue for cancer research.

Body: report for the entire period, 1994-1999.

We have collected large numbers of breast cancer tissues from patient undergoing surgery at Duke Hospital. In most cases, more than 5 small samples were obtained from each tumor; in some cases, several grams of tissue were obtained. In 30 cases, we collected both the primary and metastatic tumor from the same patient. In the majority of cases, we collected peripheral WBC's for a sample of germline, normal DNA. The following table gives a breakdown of the racial demographics of our tissue repository:

Caucasian.....	328 patients
African American.....	112 patients
Hispanics.....	3 patients
Asian.....	3 patients

TOTAL CONSENTED.....	424 patients
----------------------	--------------

The Repository has provided sterile tumor tissue for attempts at continuous culture. Sterile tissue has also been provided to investigators who have isolated tumor infiltrating lymphocytes and characterized their reactivities. The Repository has provided more than 80 sterile tumor specimens to investigators over the past four years.

Our blood bank has grown to substantial proportions. We now have blood and WBC's from more than 600 patients. This year, we added 119 new entries to the general bank and supported blood drawing for the cancer genetics projects in the Duke SPORE in Breast Cancer. The SPORE projects are noteworthy. The DOD phlebotomy service drew blood from more than 100 patients who choose to have BRCA1 and BRCA2 testing in our research laboratory. This was confidential testing and was done at Duke for no charge. In addition, patients and families testing negative for alterations in BRCA1 or BRCA2 were approached in the SPORE to donate blood for mapping studies (looking for other susceptibility genes). These studies involved blood donations both at Duke, in the field at family reunions or in private homes and through the mail. The DOD phlebotomy service has supported these efforts and our technologist accompanied the SPORE investigators in trips to collect blood from family members. I would estimate that at least 100 bloods were obtained from patients in families entered into the mapping projects. The following table gives the racial demographics our blood repository.

Caucasian.....	525
African American.....	108
Asian.....	14
Hispanic.....	5

TOTAL COLLECTION	652 patients
(not including blood drawn for special projects)	

The use of the Repository has been very brisk. Blood has gone to more than 10 investigators at Duke and several requests have been answered from laboratories outside of Duke. For instance, more than 150 samples went to Dr. Robert Ochs at the Scripps Institute in California. Dr. Ochs and his collaborators are looking at the autoimmune reaction seen frequently in patients with breast cancer. Dr. Alexander Miron at Duke has looked at E2F transcription factor mutations in primary breast cancers and in germline DNA. He has used several hundred samples of both blood and tumor tissue. Finally, Dr. Andrew Futreal has analyzed polymorphisms in candidate genes associated with breast cancer risk and he also collaborated with medical oncologists to look at determinate alleles in response to chemotherapy.

The use of tumor tissue has been equally brisk. Dr. Jeffrey Marks in the Breast Program at Duke has used more than 1100 samples of breast cancer over the past four years for a variety of projects. The most notable were collaborations with Andrew Futreal at the NIEHS and later at Duke to characterize somatic mutations of BRCA1 and BRCA2 in sporadic breast cancers. This work is highly visible and widely quoted. Dr. Marks is currently studying the best way to amplify and preserve cDNA and genomic DNA from microdissected breast cancer tissue. Again, this work depends entirely upon the availability of high quality breast cancer tissue. To date, we have distributed several thousand samples of breast cancer to more than 20 investigators at Duke and to investigators at six outside institutions.

As noted above, the most significant reflection of the quality of the work done by the Repository is its ability to be self-sufficient in the future. We successfully competed for a SPORE in Breast Cancer in 1994 and recently re-competed the SPORE for a supplemental two years of funding. This will provide funds to maintain the tissue bank and hopefully expand the blood and white cell resource. We have sought funding from industrial collaborators for an even more ambitious blood-tissue collection facility at Duke. The Comprehensive Cancer Center at Duke recently completed its competitive review. The tissue collection and banking facilities of the Center were highly rated and funded in their entirety. This will include support for the breast cancer tissue bank. The Cancer Center also added the Breast Program as a standing program of research within the Center. In large measure, this recognition was based upon the infrastructure built up at Duke over the past four or five years.

Key Research Accomplishments

- 424 patients consented for tissue samples
- 652 patients consented for blood samples
- collaborations with Dr. Robert Ochs, Dr. Alexander Miron, Dr. Andrew Futreal
- collaboration with Abbott Laboratories

Reportable Outcomes

- tissue samples from 424 patients
- blood samples from 652 patients
- Planning grant funded
- SPORE in breast cancer funded and renewed
- Cancer Genetics Network site funded
- Standing Program of Research in Duke Comprehensive Cancer Center
- Early Detection Research Network collaboration with Abbot Laboratories funded

Conclusion

The Breast Cancer Tissue Repository at Duke University has been invaluable to building our program in breast cancer research. This has resulted in a Planning Grant, a SPORE in Breast Cancer, a Cancer Genetics Network grant, funding of a new standing Program of Research in the Duke Comprehensive Cancer Center and funding of an Early Detection Research Network collaboration with Abbott Laboratories. Use has been brisk and several seminal contributions have been made to breast cancer biology.

References NA

Appendices NA

Final Report

Bibliography/publications, meeting abstracts: NA

Personnel receiving pay from this research effort:

Nancy Glover – Research Technician

Elizabeth Wildermann - Phlebotomist